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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,766	11/12/2004	Pascal Bigey	37991-0032	3543

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,766	BIGEY ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted as below:

Group I, claim(s) 1-3, 7-16, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is **bleomycin.**

Group II, claim(s) 1-2, 4, 7-15, 17, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is **an antineoplastic agent capable of methylating DNA.**

Group III, claim(s) 1-2, 5, 7-15, 18, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is a **chloroethylating agent**.

Group IV, claim(s) 1-2, 6-15, 19, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is a **cytolytic agent**.

Group V, claim(s) 1-2, 6-15, 20-23, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is a **pro-apoptotic agent.**

Group VI, claim(s) 1-2, 6-15, 24-27, and 29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is an **antimetabolite agent.**

Group VII, claim(s) 1-2, 6-15, and 28-29, drawn to a combination product comprising an antisense targeted against MBD2 demethylase and an agent used in antitumor chemotherapy for treatment of proliferative and inflammatory diseases, wherein said agent is an **antimitotic agent.**

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions of groups I-VII are found to have no special technical feature that define a contribution over the prior art of WO 99/24583 (Szyf et al., Reference A01, Form PTO 1449A, filed by applicants on December 1, 2005), in view of Cancerweekly Plus (September 1, 1997, page 34, titled as Antisense Technology; "Antitumor Activity of a C-raf Antisense Oligonucleotide in Combination with Standard Chemotherapeutic Agents Against Various Human Tumors Transplanted Subcutaneously into Nude Mice"). WO 99/24583 teaches a use of a DNA demethylase enzyme, later named MBD2, as a template to design antisense

oligonucleotides as a therapeutic agent to inhibit tumor growth (pages 6-7 of the specification). Cancerweekly Plus teaches superadditive antitumor effects *in vivo* in mice when an antisense oligonucleotide is combined with standard chemotherapeutic agents. Therefore, applicant's inventions of the combination product comprising an antisense oligonucleotide of the gene encoding MBD2 demethylase and one agent used in antitumor chemotherapy does not contribute a special technical feature when viewed over the prior art. Accordingly, they do not have a single inventive concept and so lack unity of invention, thus restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Election of Species

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:
a) streptozotocin, procarbazine, dacarbazine and temozolomide of claim 17, **drawn to generic claim 4 of group II** ;

b) 1-(2-chloroethyl)-3-(2-hydroxyethyl)-1-nitrosourea, 1-(chloroethyl)-3-(2-hydroxyethl)-1-nitrosourea, 1,3-bis(2-chloroethyl)-1-nitrosourea, 1-(2-chloroethyl)-3-(4-amino-2-methyl-5-pyrimidinyl)methyl 1-nitrosourea, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea, 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea, 1-[N-(2-chloroethyl)-N-nitrosoureido]ethylphosphonic acid diethyl ester, and 2-chloroethylmethylsulfonylmethanesulfonate of claim 18, **drawn to generic claim 5 of group III**;

c) dacarbazine, hydroxycarbamide, asparaginase, mitoguazone and plicamycin of claim 19, **drawn to generic claim 6 of group IV**;

d) glucocorticoid derivatives, topoisomerase 2 inhibitors and topoisomerase 1 inhibitors of claim 20, wherein said topoisomerase 2 inhibitor is an anthracycline epipodophyllotoxin that is etoposide, and wherein said topoisomerase 1 inhibitor is a camptothecin derivative, **drawn to generic claim 6 of group V**;

e) antifolates, antipurines, and antipyrimidines of claim 24, wherein said antifolate is methotrexate, said antipurine is 6-mercaptopurine, and said antipyrimidine is 5-fluorouracil, **drawn to generic claim 6 of group VI**;

f) and vincaalkaloids and taxoids of claim 28, **drawn to generic claim 6 of group VII**.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be

met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed antitumor agents, the Marksuh group shall be regarded as being of similar nature when

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e, a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant antitumor agents are considered to be each separate invention for the following reasons:

As described above, the antitumor agents do not meet the criteria of (A), common property or activity or (B)(1), common structure or (B)(2), art recognized class of compounds. Although all agents disclosed as potential antitumor agents have disruptive effects on cellular growth, each agent behaves in a different way in the context of the claimed invention because each agent targets a different and specific cellular or molecular pathway and thus act differently. Each member of the class cannot be substituted one for the other, with the expectation that the same intended result would be achieved.

Further, although the agents disclosed in the claims may be used in chemotherapy, the agents do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the agents is lacking and each agent claimed is considered to constitute a special technical feature.

Applicant is required, in reply to this action, to elect a single species, a single compound from one antitumor agent genus that corresponds to the elected group, to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:
a) 15 consecutive nucleotides of SEQ ID NO:1 or complementary thereto or a sequence capable of hybridizing with SEQ ID NO:1 or complementary thereto of claim 2;
b) 15 consecutive nucleotides of SEQ ID NO:2 or a sequence capable of hybridizing with SEQ ID NO of claim 2.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The nucleotides of SEQ ID NO:1 do not have common core structure with those of SEQ ID NO:2. Although SEQ ID NO:1 encompasses SEQ ID NO:2, these two SEQ IDs are unique, because nucleotides 1 – 600 of SEQ ID NO:1 are not shared by SEQ ID NO:2. Although both SEQ ID NOs:1 and 2 encode MBD2, these two sequences are unique due to the presence of non-overlapping, non-complementary nucleic sequences between the two.

Applicant is required, in reply to this action, to elect a single species, either SEQ ID NO:1 (listed as "a" above) or SEQ ID NO:2 (listed as "b" above), to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Inventorship

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Dana Shin
Examiner
Art Unit 1635

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER